# SYNTHESIS OF PHTHALIDEISOQUINOLINE ALKALOIDS AND OF OTHER ANTAGONISTS OF γ-AMINOBUTYRIC ACID.

A THESIS

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## SUMMARY

The syntheses of several classes of compounds with known central nervous system activity are described, with particular regard to those which were thought to act as antagonists of γ-aminobutyric acid.

Various new methods for the synthesis of the phthalideisoquinoline alkaloids are described in chapter I. The most successful route involved the coupling of an electrophilic isoquinoline moiety with the nucleophilic phthalide anion. This procedure provides a quick and efficient synthesis of the naturally occurring alkaloid cordrastine and also the synthesis of several other previously unreported phthalideisoquinolines. Another method which led to the phthalideisoquinoline skeleton involved the electrophilic substitution of the Reissert anion by the 3-substituted phthalide. The use of an electrophilic phthalide has not previously been successfully employed for phthalideisoquinoline synthesis.

In chapter II the synthesis of 3-aminoalkylphthalides is considered. Of the five potential synthetic approaches three were tested in the laboratory. The most successful involved a reaction of the electrophilic phthalaldehydic acid with the arylpropan-2-one and subsequent elaboration to the desired amine. This method enables the preparation of substituted analogues, except those containing a strongly electron-donating group in the para position of the non-phthalidyl aromatic ring.

Chapter III describes the synthesis of 3-, 6- and 7- substituted caprolactams. Most of these compounds were prepared by the Schmidt

rearrangement of the corresponding ketone. A detailed investigation of the rearrangement of these ketones and of arylpropan-2-ones has shown that the ratio of the two possible amide products in each case can vary when any one of the following factors: solvent, temperature and substitution pattern, is changed.

## STATEMENT

This thesis contains no material previously submitted for a degree or diploma in any university, and to the best of my knowledge and belief, contains no material previously written or published except where due reference is made in the text.

J.M. TIPPETT

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